

1. *In vivo Model of Cardiac Hypertrophy*

Rats with left ventricular hypertrophy (LVH) are produced essentially as described in Schunkert *et al.*, J. Clin. Invest. **86**(6):1913-20 (1990). LVH is induced by pressure overload as a result of constriction of the ascending aorta. A stainless steel clip of 0.6-mm internal diameter is placed on the aorta of anesthetized weanling rats. Control animals undergo thoractomy as a sham operation. Animals usually recover from surgery and appear healthy until about 20 weeks when a few animals may be in demise likely due to heart failure, which typically occurs at this point (Schunkert *et al.*, 1990, *supra*). The animals are sacrificed and hearts examined 10 weeks and 20 weeks post-operation. Hypertrophy is evident at both time points as determined by changes in left ventricle weight and thickness. Aortic banded rats and sham operated control animals are sacrificed and measured for heart weight, left ventricle (LV) weight, left ventricle thickness, and LV weight/body weight. Usually there are 6 animals per group. Data are expressed as average with standard deviation.

LVH rats are also examined for expression of ANP, BNP, cardiac  $\alpha$ -actin, and/or  $\beta$ -myosin heavy chain mRNA, using Northern blot. Levels of these messages are expected to be elevated in the diseased animals, confirming that the banded rats were pressure overloaded and responded with cardiac hypertrophy. Poly A<sup>+</sup> mRNA is prepared from each of the animals for assessment of differentially expressed genes in the disease state, using microarray analysis in a preferred embodiment.

2. *In vivo Model of Viral Myocarditis*

CVB3 infection in mice results in myocardial disease progression, which can be used as a model for examination of the pathogenesis of virus-induced human myocarditis. The virus is directly injurious to myocardial cells early following infection during the preinflammatory period as determined by light and electron microscopic cytological assessment (Arola *et al.*, J. Med. Virol. **47**: 251-259 [1995]; Chow *et al.*, Lab. Invest. **64**: 55-64 [1991]; McManus *et al.*, Clin. Immunol. Immunopathol. **68**:159-169 [1993]; Melnick *et al.*, J. Expert. Med. **93**: 247-266 [1951]). Beginning by day two post-infection cytopathic lesions are evident in ventricular myocytes, characterized by cell vacuolar changes, contraction bands and coagulation necrosis (McManus *et al.*, *supra*). By day 5 post-infection this myocardial injury becomes obscured by inflammatory infiltrates, cellular calcification, and tissue edema.

In a typical protocol, A/J (*H-2<sup>a</sup>*) mice (Jackson Laboratories, Bar Harbor, Maine, 4 weeks of age) are acclimated for one week prior to the onset of the experiment. Any mice that dies naturally during the course of the disease are not included in groups of mice to be used for RNA extraction. Mice are euthanized by CO<sub>2</sub> narcosis.

Myocarditic CVB3 (Dr. Charles J. Gauntt; University of Texas, San Antonio, Texas) is stored at -80°C. Virus is propagated in HeLa cells (American Type Tissue Culture Collection, Rockville, MD.) and is routinely titred before the onset of all experiments using the plaque assay method, with modifications as previously described (Anderson *et al.*, J. Virol. **70**: 4632-4645 [1996]).

Adolescent A/J mice are infected with  $1 \times 10^5$  pfu of myocarditic CVB3 or PBS sham and euthanized on days 3, 9, and 30 post-infection. Ten to fifteen mice per group (CVB3 infected or sham injected) per time-point (days 3, 9, and 30) are euthanized and heart muscle is removed. Following a wash in sterile phosphate buffered saline, a small portion of the apex of the heart is removed and fixed in 4% paraformaldehyde. The remainder of the heart is flash frozen in liquid nitrogen and stored at  $-80^\circ\text{C}$  for future RNA isolation.

Sections from the heart are fixed in fresh DPBS-buffered 4% paraformaldehyde overnight at  $4^\circ\text{C}$ . Fixed tissue is dehydrated in graded alcohols, cleared in xylene, embedded in paraffin, and sectioned for hematoxylin and eosin, and Masson's trichrome stains. Serial sections are also prepared for *in situ* hybridization and nick-end labelling stained. The extent and severity of virus-induced injury (including coagulation necrosis, contraction band necrosis, and cytopathic effects), inflammation, and tissue fibrosis and calcification are evaluated and scored as previously described (Chow *et al.*, *supra*).

*In situ* hybridization for CVB3 viral RNA localization is carried out as previously described (Anderson *et al.*, *supra*; Hohenadl *et al.*, Mol. Cell. Probes 5: 11-20 [1991]). Briefly, tissue sections are incubated overnight in hybridization mixture containing digoxigenin-labelled, CVB3 strand-specific riboprobes. Post-hybridization washing is followed by blocking with 2% normal lamb serum. A sheep anti-digoxigenin polyclonal antibody conjugated to alkaline phosphatase (Boehringer Mannheim PQ, Laval, Canada) is developed in Sigma-Fast nitroblue tetrazolium-BCIP [5-bromo-4-chloro-3-indolylphosphate tuluidinium] (Sigma Chemical Co.). The slides are counterstained in fresh carmalum and examined for reaction product by light microscopy. Poly A<sup>+</sup> mRNA is prepared from each of the animals, as described herein, for assessment of differentially expressed genes in the disease states, using microarray.

### 3. *In Vivo Model of Kidney Disease*

In yet another representative example, an *in vivo* model of kidney disease is used to further characterize the differentially expressed genes of the present invention. For example, a rat model of an inherited form of autosomal dominant polycystic kidney disease (ADPKD) can be used, which develops in Han:SPRD rats (Kaspereit-Rittinghaus *et al.*, Transplant Proc. 6: 2582-3 [1990]; Cowley *et al.*, Kidney Int. 43:522-34 [1993]). Renal cysts and renal failure is evident in six months old male heterozygous rats (Cy/+), whereas control rats (+/+) show no sign of cysts or renal failure. Diseased (Cy/+) and normal (+/+) animals are sacrificed and the kidneys removed. For cDNA microarray analysis, poly A<sup>+</sup> mRNA is prepared, as described previously, for assessment of differentially expressed genes in the disease state, using microarray analysis in a preferred embodiment.

All references cited throughout the specification, including the examples, are hereby expressly incorporated by reference.

## CLAIMS:

1. An isolated nucleic acid molecule comprising a poly- or oligonucleotide selected from the group consisting of:

(a) a polynucleotide encoding a polypeptide having at least about 80% sequence identity with any amino acid sequence selected from the group consisting of: amino acids 1 to 193 of SEQ ID NO: 4, amino acids 1 to 236 of SEQ ID NO:6, amino acids 1 to 61 of SEQ ID NO: 8, amino acids 1 to 92 of SEQ ID NO:12, amino acids 1 to 86 of SEQ ID NO:14, amino acids 1 to 36 of SEQ ID NO:16, amino acids 1 to 83 of SEQ ID NO:18, amino acids 1 to 82 of SEQ ID NO:20, amino acids 1 to 462 of SEQ ID NO:22, amino acids 1 to 170 of SEQ ID NO:24, amino acids -26 to 233 of Fig. 13 (amino acids 1 to 259 of SEQ ID NO: 26), amino acids 1 to 30 of SEQ ID NO:28, amino acids 1 to 30 of SEQ ID NO:35, amino acids 1 to 100 of SEQ ID NO:37, amino acids 1 to 65 of SEQ ID NO:39, amino acids 1 to 46 of SEQ ID NO:43, amino acids 1 to 313 of SEQ ID NO:46, amino acids 1 to 58 of SEQ ID NO:51, amino acids -35 to 387 of Fig. 29 (amino acids 1 to 422 of SEQ ID NO: 53), amino acids 1 to 58 of SEQ ID NO:55, amino acids 1 to 52 of SEQ ID NO:57, amino acids 1 to 245 of SEQ ID NO:59, amino acids 1 to 142 of SEQ ID NO:63, amino acids 1 to 49 of SEQ ID NO:67, amino acids 1 to 70 of SEQ ID NO:69, amino acids 1 to 113 of SEQ ID NO: 72, and amino acids 1 to 97 of SEQ ID NO:76; or a transmembrane domain (membrane spanning segment/region) deleted or inactivated variant thereof;

(b) a polynucleotide encoding a polypeptide of amino acids 1 to 233 of SEQ ID NO: 26, or amino acids 1 to 387 of SEQ ID NO: 53;

(c) a polynucleotide encoding amino acids 1 to 203 of SEQ ID NO: 2, amino acids 1 to 193 of SEQ ID NO: 4, amino acids 1 to 236 of SEQ ID NO:6, amino acids 1 to 61 of SEQ ID NO: 8, amino acids 1 to 79 of SEQ ID NO:10, amino acids 1 to 92 of SEQ ID NO:12, amino acids 1 to 86 of SEQ ID NO:14, amino acids 1 to 36 of SEQ ID NO:16, amino acids 1 to 83 of SEQ ID NO:18, amino acids 1 to 82 of SEQ ID NO:20, amino acids 1 to 462 of SEQ ID NO:22, amino acids 1 to 170 of SEQ ID NO:24, amino acids -26 to 233 of Fig. 13 (amino acids 1 to 259 of SEQ ID NO:26), amino acids 1 to 30 of SEQ ID NO:28, amino acids 1 to 39 of SEQ ID NO:30, amino acids 1 to 541 of SEQ ID NO: 33, amino acids 1 to 30 of SEQ ID NO:35, amino acids 1 to 100 of SEQ ID NO:37, amino acids 1 to 65 of SEQ ID NO:39, amino acids 1 to 42 of SEQ ID NO:41, amino acids 1 to 46 of SEQ ID NO:43, amino acids 1 to 313 of SEQ ID NO:46, amino acids 1 to 58 of SEQ ID NO:51, amino acids -35 to 387 of Fig. 29 (amino acids 1 to 422 of SEQ ID NO:53), amino acids 1 to 58 of SEQ ID NO:55, amino acids 1 to 52 of SEQ ID NO:57, amino acids 1 to 245 of SEQ ID NO:59, amino acids 1 to 142 of SEQ ID NO:63, amino acids 1 to 49 of SEQ ID NO:67, amino acids 1 to 70 of SEQ ID NO:69, amino acids 1 to 113 of SEQ ID NO: 72, and amino acids 1 to 114 of SEQ ID NO:74, and amino acids 1 to 97 of SEQ ID NO:76; or a transmembrane domain (membrane spanning segment/region) deleted or inactivated variant thereof.

(d) a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 1, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00184\_D11 (SEQ ID NO: 1), a polynucleotide hybridizing

under stringent conditions with the complement of the coding region of SEQ ID NO: 3, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00185\_D11 (SEQ ID NO: 3); a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 5, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00188\_D12 (SEQ ID NO: 5), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 7, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00188\_E01 (SEQ ID NO: 7), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 9, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00194\_G01 (SEQ ID NO: 9), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 11, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00194\_G05 (SEQ ID NO: 11), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 13, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00194\_H10 (SEQ ID NO: 13), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 15, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00199\_D08 (SEQ ID NO: 15), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 17, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00203\_D04 (SEQ ID NO: 17), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 19, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00203\_E06 (SEQ ID NO: 19), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 21, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00209\_F06 (SEQ ID NO: 21), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 23, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00219\_D02 (SEQ ID NO: 23), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 25, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00219\_F06 (SEQ ID NO: 25), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 27, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00220\_H05 (SEQ ID NO: 27), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 29, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00222\_G03 (SEQ ID NO: 29),

a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 31 (clone P00223\_F07), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 32, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00225\_C01 (SEQ ID NO: 32),

5 a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 34, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00227\_D11 (SEQ ID NO: 34), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 36, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by

10 clone P00228\_F03 (SEQ ID NO: 36), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 38, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00233\_H08 (SEQ ID NO: 38), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 40, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the

15 polypeptide encoded by clone P00235\_G08 (SEQ ID NO: 40), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 42, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00239\_C11 (SEQ ID NO: 42), a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 44 (clone P00240\_B04), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 45, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by

20 clone P00240\_E05 (SEQ ID NO: 45), a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 47 (clone P00241\_E12), a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 48 (clone P00245\_D06), a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 49 (clone P00246\_D12), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 50, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone

25 P00247\_A04 (SEQ ID NO: 50), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 52, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00248\_B04 (SEQ ID NO: 52), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 54, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00249\_F09 (SEQ ID NO: 54), a polynucleotide hybridizing under stringent

30 conditions with the complement of the coding region of SEQ ID NO: 56, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00258\_A10 (SEQ ID NO: 56), a polynucleotide hybridizing under stringent conditions with the

complement of the coding region of SEQ ID NO: 58, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00262\_C10 (SEQ ID NO: 58), a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 60 (clone P00263\_G06), a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 61 (clone P00267\_F08), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 62, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00269\_H08 (SEQ ID NO: 62), a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 64 (clone P00312\_C04), a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 65 (clone P00324\_H02), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 66, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00628\_H02 (SEQ ID NO: 66), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 68, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00629\_C08 (SEQ ID NO: 68), a polynucleotide hybridizing under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 70 (clone P00634\_G11), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 71, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00641\_G11 (SEQ ID NO: 71), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 73, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00648\_E12 (SEQ ID NO: 73), a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO: 75, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00697\_C03 (SEQ ID NO: 75);

(e) a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 148 of SEQ ID NO: 2, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00184\_D11 (SEQ ID NO: 1), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 193 of SEQ ID NO: 4, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00185\_D11 (SEQ ID NO: 3); a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 236 of SEQ ID NO: 6, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00188\_D12 (SEQ ID NO: 5), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 61 of SEQ ID NO: 8, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00188\_E01 (SEQ ID NO: 7), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 79 of SEQ ID NO: 10, wherein said polynucleotide encodes

a polypeptide having at least one biological activity of the polypeptide encoded by clone P00194\_G01 (SEQ ID NO: 9), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 92 of SEQ ID NO: 12, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00194\_G05 (SEQ ID NO: 11), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 86 of SEQ ID NO: 14, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00194\_H10 (SEQ ID NO: 13), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 36 of SEQ ID NO: 16, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00199\_D08 (SEQ ID NO: 15), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 83 of SEQ ID NO: 18, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00203\_D04 (SEQ ID NO: 17), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 82 of SEQ ID NO: 20, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00203\_E06 (SEQ ID NO: 19), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 462 of SEQ ID NO: 22, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00209\_F06 (SEQ ID NO: 21), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 170 of SEQ ID NO: 24, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00219\_D02 (SEQ ID NO: 23), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids -26 to 233 of Fig. 13 (amino acids 1 to 259 of SEQ ID NO: 26), wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00219\_F06 (SEQ ID NO: 25), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 30 of SEQ ID NO: 28, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00220\_H05 (SEQ ID NO: 27), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 39 of SEQ ID NO: 30, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00222\_G03 (SEQ ID NO: 29), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 541 of SEQ ID NO: 33, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00225\_C01 (SEQ ID NO: 32), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 30 of SEQ ID NO: 35, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00227\_D11 (SEQ ID NO: 34), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 100 of SEQ ID NO: 37, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00228\_F03 (SEQ ID NO: 36), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 65 of SEQ ID NO: 39, wherein said polynucleotide encodes

a polypeptide having at least one biological activity of the polypeptide encoded by clone P00233\_H08 (SEQ ID NO: 38), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 41 of SEQ ID NO: 39, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00235\_G08 (SEQ ID NO: 40), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 46 of SEQ ID NO: 43, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00239\_C11 (SEQ ID NO: 42), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 313 of SEQ ID NO: 46, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00240\_E05 (SEQ ID NO: 45), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 58 of SEQ ID NO: 51, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00247\_A04 (SEQ ID NO: 50), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids -35 to 387 of Fig. 29 (amino acids 1 to 422 of SEQ ID NO: 53), wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00248\_B04 (SEQ ID NO: 52), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 58 of SEQ ID NO: 55, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00249\_F09 (SEQ ID NO: 54), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 52 of SEQ ID NO: 57, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00258\_A10 (SEQ ID NO: 56), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 245 of SEQ ID NO: 59, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00262\_C10 (SEQ ID NO: 58), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 142 of SEQ ID NO: 63, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00269\_H08 (SEQ ID NO: 62), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 49 of SEQ ID NO: 67, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00628\_H02 (SEQ ID NO: 66), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 70 of SEQ ID NO: 69, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00629\_C08 (SEQ ID NO: 68), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 113 of SEQ ID NO: 72, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00641\_G11 (SEQ ID NO: 71), a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 114 of SEQ ID NO: 74, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00648\_E12 (SEQ ID NO: 73), a polynucleotide encoding at least about 50 contiguous amino acids



from amino acids 1 to 97 of SEQ ID NO: 76, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00697\_C03 (SEQ ID NO: 75);

(f) a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 1 to 23 of SEQ ID NO: 26, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00219\_F06 (SEQ ID NO: 25) or amino acids 1 to 387 of SEQ ID NO: 53, wherein said polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by clone P00248\_B04 (SEQ ID NO: 52);

(g) a polynucleotide of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 32, 34, 36, 38, 40, 42, 44, 45, 47, 48, 49, 50, 52, 54, 56, 58, 60, 61, 62, 64, 65, 66, 68, 70, 71, 73, and 75;

(h) the complement of a polynucleotide of (a) – (g); and

(i) an antisense oligonucleotide capable of hybridizing with, and inhibiting the translation of, the mRNA encoded by a gene encoding a polypeptide of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 33, 35, 37, 39, 41, 43, 46, 51, 53, 55, 57, 59, 63, 67, 69, 72, 74, 76, or another mammalian homologue thereof.

2. The polynucleotide of claim 1 encoding a polypeptide comprising amino acids 1 to 233 of SEQ ID NO: 26, amino acids 1 to 387 of SEQ ID NO: 53.

3. The polynucleotide of claim 1 comprising the sequence selected from the group consisting of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 32, 34, 36, 38, 40, 42, 44, 45, 47, 48, 49, 50, 52, 54, 56, 58, 60, 61, 62, 64, 65, 66, 68, 70, 71, 73, and 75.

4. A vector comprising and capable of expressing a poly- or oligonucleotide of claim 1.

5. A recombinant host cell transformed with nucleic acid comprising a poly- or oligonucleotide of claim 1.

6. A recombinant host cell transformed with the vector of claim 5.

7. A method for producing a polypeptide comprising culturing a recombinant host cell transformed with nucleic acid comprising any of the polynucleotides of claim 1(a) – (g) under conditions such that the polypeptide is expressed, and isolating the polypeptide.

8. A polypeptide comprising:

(a) a polypeptide having at least about 80% identity with amino acids selected from the group consisting of: amino acids 1 to 193 of SEQ ID NO: 4, amino acids 1 to 236 of SEQ ID NO:6, amino acids 1 to 61 of SEQ ID NO: 8, amino acids 1 to 92 of SEQ ID NO:12, amino acids 1 to 86 of SEQ ID NO:14, amino acids 1 to 36 of SEQ ID NO:16, amino acids 1 to 83 of SEQ ID NO:18, amino acids 1 to 82 of SEQ ID NO:20, amino acids 1 to 462 of SEQ ID NO:22, amino acids 1 to 170 of SEQ ID NO:24, amino acids 1 to 30 of SEQ ID NO:28, amino acids 1 to 30 of SEQ ID NO: 35, amino acids 1 to 100 of SEQ ID NO:37, amino acids 1 to 65 of SEQ ID NO:39, amino acids 1 to 46 of SEQ ID NO:43, amino acids 1 to 313 of SEQ ID NO:46, amino acids 1 to 58 of SEQ ID NO:51, amino acids 1 to 58 of SEQ ID NO:55, amino acids 1 to 52 of SEQ ID NO:57, amino acids 1 to 245 of SEQ ID NO:59, amino acids 1 to 142 of SEQ ID NO:63,

amino acids 1 to 49 of SEQ ID NO:67, amino acids 1 to 70 of SEQ ID NO:69, amino acids 1 to 113 of SEQ ID NO:72, and amino acids 1 to 97 of SEQ ID NO:76; or

(b) a polypeptide encoded by nucleic acid hybridizing under stringent conditions with the complement of the coding region selected from the group consisting of: SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 32, 34, 36, 38, 40, 42, 44, 45, 47, 48, 49, 50, 52, 54, 56, 58, 60, 61, 62, 64, 65, 66, 68, 70, 71, 73, and 75;

(c) the polypeptides of (a) and (b) having at least one biological activity of the polypeptide encoded by clones P00184\_D11 (SEQ ID NO:1), P00185\_D11(SEQ ID NO:3), P00188\_D12 (SEQ ID NO:5), P00188\_E01 (SEQ ID NO:7), P00194\_G01 (SEQ ID NO:9), P00194\_G05 (SEQ ID NO:11), P00194\_H10 (SEQ ID NO:13), P00199\_D08 (SEQ ID NO:15), P00203\_D04 (SEQ ID NO:17), P00203\_E06 (SEQ ID NO:19), P00209\_F06 (SEQ ID NO:21), P00219\_D02 (SEQ ID NO:23), P00219\_F06 (SEQ ID NO:25), P00220\_H05 (SEQ ID NO:27), P00222\_G03 (SEQ ID NO:29), P00225\_C01 (SEQ ID NO:32), P00227\_D11 (SEQ ID NO:34), P00228\_F03 (SEQ ID NO:36), P00233\_H08 (SEQ ID NO:38), P00235\_G08 (SEQ ID NO:40), P00239\_C11 (SEQ ID NO:42), P00240\_E05 (SEQ ID NO:45), P00247\_A04 (SEQ ID NO:50), P00248\_B04 (SEQ ID NO:52), P00249\_F09 (SEQ ID NO:54), P00258\_A10 (SEQ ID NO:56), P00262\_C10 (SEQ ID NO:58), P00269\_H08 (SEQ ID NO:62), P00628\_H02 (SEQ ID NO:66), P00629\_C08 (SEQ ID NO:68), P00641\_G11 (SEQ ID NO:71), P00648\_E12 (SEQ ID NO:73), P00697\_C03 (SEQ ID NO:75).

9. A composition comprising a polypeptide which comprises:

(a) a polypeptide having at least about 80% identity with amino acids selected from the group consisting of: amino acids 1 to 193 of SEQ ID NO: 4, amino acids 1 to 236 of SEQ ID NO:6, amino acids 1 to 61 of SEQ ID NO: 8, amino acids 1 to 92 of SEQ ID NO:12, amino acids 1 to 86 of SEQ ID NO:14, amino acids 1 to 36 of SEQ ID NO:16, amino acids 1 to 83 of SEQ ID NO:18, amino acids 1 to 82 of SEQ ID NO:20, amino acids 1 to 462 of SEQ ID NO:22, amino acids 1 to 170 of SEQ ID NO:24, amino acids 1 to 30 of SEQ ID NO:28, amino acids 1 to 30 of SEQ ID NO: 35, amino acids 1 to 100 of SEQ ID NO:37, amino acids 1 to 65 of SEQ ID NO:39, amino acids 1 to 46 of SEQ ID NO:43, amino acids 1 to 313 of SEQ ID NO:46, amino acids 1 to 58 of SEQ ID NO:51, amino acids 1 to 58 of SEQ ID NO:55, amino acids 1 to 52 of SEQ ID NO:57, amino acids 1 to 245 of SEQ ID NO:59, amino acids 1 to 142 of SEQ ID NO:63, amino acids 1 to 49 of SEQ ID NO:67, amino acids 1 to 70 of SEQ ID NO:69, amino acids 1 to 113 of SEQ ID NO:72, and amino acids 1 to 97 of SEQ ID NO:76; or

(b) a polypeptide encoded by nucleic acid hybridizing under stringent conditions with the complement of the coding region selected from the group consisting of: SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 32, 34, 36, 38, 40, 42, 44, 45, 47, 48, 49, 50, 52, 54, 56, 58, 60, 61, 62, 64, 65, 66, 68, 70, 71, 73, and 75; wherein the polypeptides of (a) and (b) have at least one biological activity of the polypeptide respectively encoded by clones P00184\_D11 (SEQ ID NO:1), P00185\_D11(SEQ ID NO:3), P00188\_D12 (SEQ ID NO:5), P00188\_E01 (SEQ ID NO:7), P00194\_G01 (SEQ ID NO:9), P00194\_G05 (SEQ ID NO:11), P00194\_H10 (SEQ ID NO:13), P00199\_D08 (SEQ ID

NO:15), P00203\_D04 (SEQ ID NO:17), P00203\_E06 (SEQ ID NO:19), P00209\_F06 (SEQ ID NO:21), P00219\_D02 (SEQ ID NO:23), P00219\_F06 (SEQ ID NO:25), P00220\_H05 (SEQ ID NO:27), P00222\_G03 (SEQ ID NO:29), P00225\_C01 (SEQ ID NO:32), P00227\_D11 (SEQ ID NO:34), P00228\_F03 (SEQ ID NO:36), P00233\_H08 (SEQ ID NO:38), P00235\_G08 (SEQ ID NO:40),  
5 P00239\_C11 (SEQ ID NO:42), P00240\_E05 (SEQ ID NO:45), P00247\_A04 (SEQ ID NO:50), P00248\_B04 (SEQ ID NO:52), P00249\_F09 (SEQ ID NO:54), P00258\_A10 (SEQ ID NO:56), P00262\_C10 (SEQ ID NO:58), P00269\_H08 (SEQ ID NO:62), P00628\_H02 (SEQ ID NO:66), P00629\_C08 (SEQ ID NO:68), P00641\_G11 (SEQ ID NO:71), P00648\_E12 (SEQ ID NO:73), and P00697\_C03 (SEQ ID NO:75), in admixture with a carrier.

10 10. The composition of claim 9 which is a pharmaceutical composition comprising an effective amount of said polypeptide in admixture with a pharmaceutically acceptable carrier.

11. An antibody specifically binding a polypeptide of claim 8.

12. A composition comprising an antibody of claim 11 in admixture with a carrier.

15 13. The composition of claim 9 which is a pharmaceutical composition comprising an effective amount of said antibody in admixture with a pharmaceutically acceptable carrier.

14. A composition comprising an antagonist or an agonist of a polypeptide of claim 8.

15 15. The composition of claim 11 which is a pharmaceutical composition comprising an effective amount of said antagonist or said agonist in combination with a pharmaceutically acceptable carrier.

20 16. A method for the treatment of a cardiac, renal or inflammatory disease, comprising administering to a patient in need an effective amount of a polypeptide of claim 8, or an antagonist or agonist thereof.

25 17. A method for the treatment of a cardiac, renal or inflammatory disease, comprising administering to a patient in need an effective amount of an antibody specifically binding to a polypeptide of the present invention.

18. A method for screening a subject for a cardiac, renal or inflammatory disease characterized by the differential expression of the polypeptide selected from the group consisting of: SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 33, 35, 37, 39, 41, 43, 46, 51, 53, 55, 57, 59, 63, 67, 69, 72, 74, and 76, or an endogenous homologue thereof, comprising the steps of:

30 measuring the expression in the subject of said polypeptide or said endogenous homologue; and determining the relative expression of said polypeptide or said endogenous homologue in the subject compared to its expression in normal subjects, or compared to its expression in the same subject at an earlier stage of development of the cardiac, renal or inflammatory disease.

35 19. The method of claim 15 wherein said subject is human and said endogenous homologue is a human homologue of the rat protein selected from the group consisting of: SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 33, 35, 37, 39, 41, 43, 46, 51, 53, 55, 57, 59, 63, 67, 69, 72, 74, and 76.

20. An array comprising one or more oligonucleotides complementary to reference RNA or DNA encoding a protein selected from the group consisting of: SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 33, 35, 37, 39, 41, 43, 46, 51, 53, 55, 57, 59, 63, 67, 69, 72, 74, and 76, or another mammalian (e.g. human) homologue thereof, where the reference DNA or RNA sequences are obtained from both a biological sample from a normal subject and a biological sample from a subject exhibiting a cardiac, renal, or inflammatory disease, or from biological samples taken at different stages of a cardiac, renal, or inflammatory disease.

21. A method for detecting cardiac, kidney, or inflammatory disease in a human test patient comprising the steps of:

providing an array of oligonucleotides at known locations on a substrate, which array comprises oligonucleotides complementary to reference DNA or RNA sequences encoding a human homologue of the protein selected from the group consisting of: SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 33, 35, 37, 39, 41, 43, 46, 51, 53, 55, 57, 59, 63, 67, 69, 72, 74, and 76 where the reference DNA or RNA sequences are obtained from both a biological sample from a normal patient and a biological sample from a patient potentially exhibiting cardiac, renal, or inflammatory disease, or from a test patient exhibiting cardiac, renal, or inflammatory disease, taken at different stages of such disease;

exposing the array, under hybridization conditions, to a first sample of cDNA probes constructed from mRNA obtained from a biological sample from a corresponding biological sample of a normal patient or from a test patient at a certain stage of the disease;

exposing the array, under hybridization conditions, to a second sample of cDNA probes constructed from mRNA obtained from a biological sample obtained from the test;

quantifying any hybridization between the first sample of cDNA probes and the second sample of cDNA probes with the oligonucleotide probes on the array; and

determining the relative expression of genes encoding the human homologue of a protein selected from the group consisting of: SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 33, 35, 37, 39, 41, 43, 46, 51, 53, 55, 57, 59, 63, 67, 69, 72, 74, and 76 in the biological samples from the normal patient and the test patient, or in the biological samples taken from the test patient at different stages of the disease.

22. A diagnostic kit for the detection of a cardiac, kidney or inflammatory disease comprising an array of claim 20.

23. The diagnostic kit of claim 22 further comprising at least one of the following components:

- (a) an oligonucleotide probe;
- (b) a PCR reagent;
- (c) a detectable label;
- (d) a biological sample taken from a human subject; and

(e) an antibody to a polypeptide of any one of the sequences selected from the group consisting of: SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 33, 35, 37, 39, 41, 43, 46, 51, 53, 55, 57, 59, 63, 67, 69, 72, 74, 76, and a further mammalian homologue thereof.

24. The diagnostic kit of claim 22 wherein said biological sample is from blood or a tissue.

25. The diagnostic kit of claim 21 wherein said tissue is a cardiac tissue.

26. The diagnostic kit of claim 22 wherein said cardiac tissue is a left ventricular tissue.